DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

Chicago District
550 West Jackson Blvd., 15th Floor
Chicago, Illinois 60661
Telephone: 312-353-5863

September 24, 2002

**WARNING LETTER**
**CHI-25-02**

**CERTIFIED MAIL**
**RETURN RECEIPT REQUESTED**

Mr. Miles D.White
Chairman & CEO
Abbott Laboratories, Inc.,
One Abbott Park Road, Bldg AP6
Abbott Park, IL 60064

Dear Mr. White:

An inspection of Abbott's pharmaceutical manufacturing operations in Building AP-16, located at Abbott Park, IL, was conducted from June 18 through July 24, 2002. The inspection covered the production of [redacted] During the inspection, our investigators documented significant violations of current Good Manufacturing Practice (cGMP) regulations listed in Title 21, Code of Federal Regulations (CFR), in your firm's production of [redacted] These violations cause this product to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act).

1. Failure to conduct a thorough investigation when a batch or any of its components fail to meet specifications [21 CFR 211.192]. For example:

> During the production of [redacted] lot #79298AF00, black, magnetic particulates were observed in the granulation. The corrective action taken was to recondition the granulation by [redacted] that were expected to eliminate the particles. No validation study was performed to establish that this procedure would successfully eliminate all of the particles.
>
> During processing, lot #79298AF00 was stored in containers numbered from 1-153. After finding metal particulate contamination in tablets held in container #153, your firm's investigation covered the tablets held in container #152 only. No additional inspection of tablets held in containers #1-151 was conducted.

During the production of Erythrocin Stearate Tablets, lot #81420AF00, a metal particle was observed on the surface of one tablet held in container #8. This lot was held in a total of nine containers numbered from 1 to 9. After the remaining tablets held in container #9 were destroyed, your firm visually re-examined only the tablets held in container #8 and no re-examination of the tablets held in containers #1-7 was performed.

2. Failure to have adequate written procedures for production and process control to assure that drug products have the identity, strength, quality and purity they purport or are represented to possess [21 CFR 211.100(a)]. For example:

[redacted] Tablet lot #79298AF00 was one of the batches included in the process validation study for this product. This lot was not produced using the manufacturing process discussed in the validation study protocol. Lot #79298AF00 was subjected to several reconditioning steps, due to particulate contamination, that were not listed in the master batch record. Some of the actions taken with respect to this lot, such as the hand pouring of the granules from a drum and [redacted] were steps that were not performed for the production of the two additional [redacted] lots used in the validation study.

The master batch manufacturing instructions for the production of [redacted] differ from the procedures used in manufacturing the batches produced in the validation study. The drying process for the tablet granulation component used in the validation batches used a different type of dryer and different time and temperature parameters from the procedures directed in the master batch manufacturing.

3. Failure to clean, maintain and sanitize, at appropriate intervals, equipment and utensils used in the manufacture, processing, packing, or holding of a drug product [21 CFR 211.67(a)]. For example:

Your firm determined that black particles found in tablet granulations was due to the disintegration of the mill's drive damper and grease seals. Your firm also determined that metal particles clinging to the surface of one tablet was due to the tablet press turret rubbing the upper guard, caused by a worn Neoprene mounting pad. In both examples, there was no established schedule for inspecting or replacing these parts.

At the conclusion of the inspection, our investigators issued the FDA 483, List of Inspectional Observations, to Kay E. Peel, Vice President, Quality Assurance, PPD. A copy of the FDA 483 is enclosed.

This letter and the FDA 483 are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure that the drug products you manufacture are in compliance with the Act and the regulations promulgated under it. Federal agencies are routinely advised of Warning Letters issued so that they may take this information into account when considering the award of government contracts.

You should take prompt action to correct deficiencies at your facility. Failure to implement corrective measures may result in further regulatory action without notice. These actions may include seizure of your products or injunction.

You should notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct the deficiencies at your firm and prevent their recurrence. Your reply should be directed to the attention of George F. Bailey.

We have received Ms. Peel's written response, dated August 6, 2002, regarding the inspectional observations on the FDA 483. We note that, in response to FDA 483 item #2, Abbott has committed to running three additional validation batches of [redacted] and that a target date for completion of this activity is scheduled for October 31, 2002. Please notify this office when you have completed the additional validation batches. With regard to that commitment and the other corrective steps Ms. Peel indicates are underway or have been completed, we will consider your FDA 483 response in conjunction with any response to the Warning Letter and will determine the acceptability of your responses during a subsequent follow-up inspection.

Sincerely,

/S/

Arlyn H. Baumgarten
District Director

Enclosure: FDA 483